UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,747	09/17/2008	Yong-Mahn Han	0002838USU/4105	2538

27623 7590 03/30/2010

OHLANDT, GREELEY, RUGGIERO & PERLE, LLP
ONE LANDMARK SQUARE, 10TH FLOOR
STAMFORD, CT 06901

EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
1632	
MAIL DATE	**DELIVERY MODE**
03/30/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,747	HAN ET AL.	
	Examiner	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 April 2008* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/6/08; 2/5/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-13 are pending.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 7 require pBCKI I, pBCKI II, pBCKIDT I and pBCKIDT II, which are not readily available to the public from a reproducible source at the time of filing. Thus, a deposit of the plasmids needs to be made to meet the requirements for enablement.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the clone has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. 37 CFR 1.808.

If the deposit has <u>not</u> been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.808, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
(d) a viability statement in accordance with the provisions of 37 CFR 1,807; and
(e) the deposit will be replaced if it should ever become inviable.

As required under 37 CFR 1.809(d), the specification shall contain: (1) the accession number for the deposit; (2) the date of deposit; (3) a description of the deposited biological material sufficient to identify it and to permit its examination; and (4) the name and address of the depository.

It is noted DH5@/pBCTPOKIDT II has been deposited under the terms of the Budapest Treaty but there is no indication of compliance with 37 CFR § 1.808 and the cell line does not appear to contain any of the claimed plasmids.

Thus, at the time of the present invention, the skilled artisan would have needed to engage in an undue amount of experimentation to implement the invention as claimed.

Claims 10-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for producing a bovine β-casein targeted somatic cell , methods of generating transgenic cattle and a method for obtaining a desired protein from the milk of a cattle by a method comprising transferring a bovine donor fibroblast nucleus into a bovine enucleated oocyte and transfer to a bovine female recipient, does not reasonably provide enablement for the claims as written which are to any donor cell type, and cross species nuclear transfer.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

At the time of filing, only ES cells and fibroblasts were known to undergo sufficient population doublings for selection of transformed cell types. The fundamental problem with gene targeting of cells for nuclear transfer is that most cells only divide a limited number of times in culture and gene targeting requires that the few cells that actually take up the targeting construct must be permitted to grow (divide) until there are sufficient cells (Pennisi and Vogel (2000), page 1723, col. 3, parag. 1, lines 5-16). Also at the time of filing cross species nuclear transfer was unpredictable in that the different species could not support fetal development to term of other species embryos. Thus at the time of the instant invention the skilled artisan would have needed to engage in an undue amount of experimentation to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8 and 9 are confusing as to the location of the somatic cell and embryo. It isn't clear if applicant means the cell or embryo is in an intact bovine. A suggestion is to insert “isolated” before bovine to indicate the cell or embryo is “isolated.” Further the term “β-casein gene targeted” is confusing and unclear. A suggested rewrite is "an isolated bovine somatic produced by introducing the vector of claim 1-5 into an isolated bovine somatic cell and permitting the insertion of the DNA construct of the vector into

the endogenous β-casein gene" and "an isolated bovine embryo produced by introducing the nucleus of the somatic cell of claim 8 into an enucleated oocyte to produce a bovine embryo."

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 rejected under 35 U.S.C. 103(a) as being unpatentable over Bonsing et al. Australian Journal of Biological Sciences, 1988, Vol. 41(4), pp. 527-537; Shen et al. Chinese Journal, of Biotechnology, May 2004, Vol. 20(3), pp. 361-365 and U.S. Patent 5,843,705 issued December 1, 1998.

Bonsing teaches the genomic organization of the bovine β-casein gene including the location of the introns and exons (page 528, figure 1).

Wei teaches a goat β-casein knockin expression vector. The vector is composed of a 6.3 Kb 5' promoter fragment including exon 1 and part of exon 2 and a 2.4 Kb 3' flanking region fragment that includes exon 8 and exon 9 (abs, lines 7-11). The fragments are respectively linked to a coding sequence for ATIII inserted into a cloning sites within the vector (abs, line 13-14) The negative selectable marker neo^r and the positive selectable marker thymine kinase (tk) were inserted into the vector (abs. lines 10-11). Wei offers motivation in stating gene targeting is a powerful tool in the production of recombinant proteins in the mammary gland (abs, lines 1-4). The use of a

selectable marker gene would be obvious at the time the time of filing. In particular diphtheria toxin was well known as a selectable marker.

DiTullio teaches the insertion of cloning sites into a similar goat β-casein expression vector (col. 3, lines 59-66).

The bovine β-casein gene fragments of the cited prior art are homologous to the fragments of the claims because homologous only means similar structure, and does not confer size or sequence similarities.

Thus at the time of filing the ordinary artisan would have found it obvious to combine the cited prior art to make and use the gene targeting vector of the claims, given the specific teachings in the art and the motivation provided by Shen. Further the artisan would have readily recognized the benefit of adapting the goat vector to bovine for use in producing transgenic bovines.

Claims 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over PgPub20050177878 published August 11, 2005, efd September 30, 2003 (Melo) and further in view of over Bonsing et al. Australian Journal of Biological Sciences, 1988, Vol. 41(4), pp. 527-537; Shen et al. Chinese Journal, of Biotechnology, May 2004, Vol. 20(3), pp. 361-365 and U.S. Patent 5,843,705 issued December 1, 1998.

Melo teaches transgenic bovines produced by nuclear transfer using a bovine fibroblast as donor, where the fibroblast contained an exogenous DNA construct comprising a β-casein 5' promoter segment operably linked to a gene encoding human growth hormone (). The method requires the β-casein promoter - hGH DNA fragment to be introduced into bovine fibroblasts to produce a bovine fibroblast having the DNA

fragment integrated into its genome by negative selection (). The nucleus of the fibroblast is then transferred to an enucleated bovine oocyte activated and cultured to produce a bovine embryo comprising the DNA fragment integrated into the genome of the embryo's cells (). The embryo is transferred to a recipient bovine for term development ().Melo further teaches the isolation of hGH from the milk of the transgenic, nuclear transfer produced bovines ().

Bonsing teaches the genomic organization of the bovine β-casein gene including the location of the introns and exons (page 528, figure 1).

Wei teaches a goat β-casein knockin expression vector. The vector is composed of a 6.3 Kb 5' promoter fragment including exon 1 and part of exon 2 and a 2.4 Kb 3' flanking region fragment that includes exon 8 and exon 9 (abs, lines 7-11). The fragments are respectively linked to a coding sequence for ATIII inserted into a cloning sites within the vector (abs, line 13-14) The negative selectable marker neo^r and the positive selectable marker thymine kinase (tk) were inserted into the vector (abs. lines 10-11). Wei offers motivation in stating gene targeting is a powerful tool in the production of recombinant proteins in the mammary gland (abs, lines 1-4). The use of a selectable marker gene would be obvious at the time the time of filing. In particular diphtheria toxin was well known as a selectable marker.

DiTullio teaches the insertion of cloning sites into a similar goat β-casein expression vector (col. 3, lines 59-66).

The bovine β-casein gene fragments of the cited prior art are homologous to the fragments of the claims because homologous only means similar structure, and does not confer size or sequence similarities.

Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to produce transgenic bovines, transgenic bovine embryos, and transgenic bovine somatic cells by the methods claimed as each limitation is found in the combination of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

March 31, 2010